Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
J 7185/cm		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/005831	28.05.2004	18.06.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant		
IEP GmbH		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 11 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-36 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1-40 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 6, 7 and 16-19; claim 15 in part

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 6, 7 and 16-19; claim 15 in part

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See Supplemental Box for further details.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3-5, 8-14	YES
	Claims	1, 2, 15, 20-40	NO
Inventive step (IS)	Claims	3-5, 8, 9	YES
	Claims	1, 2, 10-15, 20-40	NO
Industrial applicability (IA)	Claims	1-5, 8-15, 20-40	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Prior art documents

In this written opinion the abbreviations **D1** to **D7** are used to refer to the searched prior art documents in the order in which they are listed in the international search report (ISR). The ISR was established by the Examining Authority.

1. Summary of the application

The application relates essentially to an NADH-dependent *S*-specific oxidoreductase with an amino acid sequence as defined by SEQ ID No. 9.

2. Novelty (PCT Article 33(2))

2.1 The subject matter of claims 3 to 5 and 8 to 14 has not been made accessible to the public by the available prior art and can therefore be considered novel.

2.2 The subject matter of claims 1, 2, 15 and 20 to 40 fails to meet the requirements of PCT Article 33(2) and (3).

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2.3 Documents **D1** (WO 93/18138), **D2** (WO 02/086126), **D3** (Jones et al.), **D4** (Xie et al.), **D5** (Schütte et al.), **D6** (Cannio et al.) and **D7** (Bayer et al.) all disclose NAD-dependent *S*-specific carbonyl reductases (see also page 1, line 20 to page 2, line 2 in the present application). In their present form claims 1 and 2 are therefore inadmissible under EPC Article 54.

2.4 The applicant is reminded that it is not permissible to use the origin of a sequence (human, mouse or, as in claim 2, "yeasts of the genus *Pichia* or *Candida*") to establish novelty over known sequences with the same structural features and the same activity. To a person skilled in the art it is not obvious, for example, whether a given NADH-dependent *S*-specific oxidoreductase is from *Pichia capsulata*, *Candida parapsilosis* or *Rhodococcus erythropolis*.

2.5 Any known nucleotide sequence that encodes an NADH-dependent *S*-specific oxidoreductase is prejudicial to the novelty of the subject matter of claim 15 (b). These known polynucleotides all hybridise with the sequences specified in claim 15 (a). It is noted that the term "strict [conditions]" is relative. Consequently the subject matter of claims 20 to 22 cannot be considered novel at this point in time.

2.6 The methods of claims 23 to 40 are indistinguishable from the methods described in **D1** (WO 93/18138) and **D2** (WO 02/086126). The subject matter of these claims cannot therefore be considered novel.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3. Inventive step (PCT Article 33(3))

3.1 The subject matter of claims 3 to 5, 8 and 9 is not obvious from the available prior art and therefore meets the requirement of PCT Article 33(3).

3.2 The subject matter of claims 10 to 14 fails to meet the requirement of PCT Article 33(3).

3.3 The subject matter of claims 10 to 12 ("fragments") contributes nothing to the inventive solution to the problem addressed by the invention (i.e. that of providing a new oxidoreductase with high enantioselectivity (*S*-specific) and a high degree of stability against organic solvents (see page 3, lines 25 to 27)). The problem addressed by the invention is not solved by the subject matter of claims 10 to 12.

3.4 The same argument applies to claims 13 and 14, which relate to an oxidoreductase as defined by SEQ ID No. 10. The sequence according to SEQ ID No. 10 is the sequence not of an oxidoreductase but rather of a 12-amino-acid-long fragment of an oxidoreductase that does not perform the specified function (see also page 4, lines 18 to 23).

4. Industrial applicability (PCT Article 33(4))

Claims 1 to 5, 8 to 15 and 20 to 40 all meet the requirement of PCT Article 33(4).

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The application as a whole lacks conciseness on account of the large number of independent claims (PCT Rule 6.1(a)).

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 1 defines oxidoreductases which reduce a carbonyl compound to the corresponding *(S)*-hydroxy compound. The activity measurement in dependent claim 4 is not consistent with this because the product is an *(R)*-hydroxy compound, not an (S)-hydroxy compound as in claim 1.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment* on _____

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

The original application includes 5 pages of sequence listing (10 sequences) (pages 1 to 5 of the description).

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No international search report was established in respect of the subject matter of claims 6, 7 and 16 to 19, or in respect of claim 15 (in part). The subject matter not covered by the search report will therefore not be dealt with in the international preliminary examination (PCT Rule 66.1(e)).

2. Claim 6 covers all oxidoreductases that are characterised by "70% or 80% identical amino acids to the amino acid sequence of SEQ ID No. 9", and further characterised in that they have 1 to 40 amino acids more or 1 to 40 amino acids less. Firstly it is completely unclear which sequences are covered by this claim (PCT Article 6), and secondly there is only a limited number of such oxidoreductases that are fully disclosed (PCT Article 5) and supported by the description (PCT Article 6). It is therefore not possible to carry out a meaningful search and examination in respect of this claim. The same applies to claim 7.

3. Claim 15 (c) relates to a polynucleotide which differs from the polynucleotides of claim 15 (a) and claim 15 (b) on account of the degeneration of the genetic code of the polynucleotides. The

reference to the degeneration of the genetic code only makes sense if the protein which the polynucleotide is supposed to encode is defined by its exact amino acid sequence. This is not the case in claim 15 (a) or claim 15 (b) (no amino acid sequence is specified; use of the term "hybridises"). It is therefore not possible to carry out a meaningful search and examination in respect of the subject matter of claim 15 (c) (PCT Article 6).

4. Claim 16 seeks to define the DNA sequence in terms of an enzyme, but the amino acid sequence of the enzyme is not defined in the claim and it is completely unclear what the DNA sequences are. The phrase "70% ..." makes the claim even more unclear. It is therefore not possible to carry out a meaningful search and examination in respect of the subject matter of claims 16 and 17 (PCT Article 6).

5. It is completely unclear what DNA sequences are defined in claim 18 ("one or more parts"). It is therefore not possible to carry out a meaningful search and examination in respect of the subject matter of claims 18 and 19 (PCT Article 6).